

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1-76. (Cancelled)

77. (Currently amended) A gene-targeted, mouse~~rodent~~ heterozygous for a human mutation of the presenilin-1 (PS-1) gene and heterozygous for an amyloid precursor protein (APP) gene of said rodent having a human FAD Swedish mutation and a humanized A $\beta$  nucleotide sequence, wherein said mutation of said PS-1 gene is P264L.

78 . (Currently amended) A gene-targeted, mouse~~rodent~~ homozygous for a human mutation of the presenilin-1 (PS-1) gene and homozygous for an amyloid precursor protein (APP) gene of said mammal having a human FAD Swedish mutation and a humanized A $\beta$  nucleotide sequence, wherein said mutation of said PS-1 gene is P264L.

79. (Currently amended) A gene-targeted, mouse~~rodent~~ homozygous for a human mutation of the presenilin-1 (PS-1) gene and heterozygous for an amyloid precursor protein (APP) gene of said mammal having a human FAD Swedish mutation and a humanized A $\beta$  nucleotide sequence, wherein said mutation of said PS-1 gene is P264L.

80. (Currently amended) A gene-targeted, mouse~~rodent~~ heterozygous for a human mutation of the presenilin-1 (PS-1) gene and homozygous for an amyloid precursor protein (APP) gene of said mammal having a human FAD Swedish mutation and a humanized A $\beta$  nucleotide sequence, wherein said mutation of said PS-1 gene is P264L.

81-88. (Cancelled)

89. (Currently amended) Generational offspring of the mouse~~rodent~~ of claim 77 wherein said mutant PS-1 gene is expressed.

90. (Currently amended) Generational offspring of the mouseredent of claim 78 wherein said mutant PS-1 gene is expressed.

91. (Currently amended) Generational offspring of the mouseredent of claim 79 wherein said mutant PS-1 gene is expressed.

92. (Currently amended) Generational offspring of the mouseredent of claim 80 wherein said mutant PS-1 gene is expressed.

93. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A $\beta$  peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouseredent of claim 77; and
- b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A $\beta$  peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A $\beta$  peptide.

94. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A $\beta$  peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouseredent of claim 78; and
- b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A $\beta$  peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A $\beta$  peptide.

95. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A $\beta$  peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouseredent of claim 79; and

b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A<sub>β</sub> peptide.

96. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A<sub>β</sub> peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouseredent of claim 80; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A<sub>β</sub> peptide.

97. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A<sub>β</sub> peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouseredent of claim 89; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A<sub>β</sub> peptide.

98. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A<sub>β</sub> peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouseredent of claim 90; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A<sub>β</sub> peptide.

99. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A<sub>β</sub> peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouse~~rodent~~ of claim 91; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouse~~rodent~~,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A<sub>β</sub> peptide.

100. (Currently amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of A<sub>β</sub> peptide, said method comprising the steps of:

- a) administering said chemical compound to the mouse~~rodent~~ of claim 92; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouse~~rodent~~,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said A<sub>β</sub> peptide.

101. (Previously presented) The method of claim 93 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

102. (Previously presented) The method of claim 94 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

103. (Previously presented) The method of claim 95 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

104. (Previously presented) The method of claim 96 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

105. (Previously presented) The method of claim 97 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

106. (Previously presented) The method of claim 98 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

107. (Previously presented) The method of claim 99 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

108. (Previously presented) The method of claim 100 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

109. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

a) administering a compound to the mouse~~rodent~~ of claim 77; and

b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouse~~rodent~~,

wherein a decrease in the amount of A $\beta$  peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

110. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

a) administering a compound to the mouse~~rodent~~ of claim 78; and

b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouse~~rodent~~,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

111. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

- a) administering a compound to the mouscrodent of claim 79; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouscrodent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

112. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

- a) administering a compound to the mouscrodent of claim 80; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouscrodent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

113. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

- a) administering a compound to the mouscrodent of claim 89; and
- b) measuring the amount of A<sub>β</sub> peptide in a tissue sample from said mouscrodent,

wherein a decrease in the amount of A<sub>β</sub> peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

114. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

- a) administering a compound to the mouseredent of claim 90; and
- b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A $\beta$  peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

115. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

- a) administering a compound to the mouseredent of claim 91; and
- b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A $\beta$  peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

116. (Currently amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

- a) administering a compound to the mouseredent of claim 92; and
- b) measuring the amount of A $\beta$  peptide in a tissue sample from said mouseredent,

wherein a decrease in the amount of A $\beta$  peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

117. (Previously presented) The method of claim 109 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

118. (Previously presented) The method of claim 110 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

119. (Previously presented) The method of claim 111 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

120. (Previously presented) The method of claim 112 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

121. (Previously presented) The method of claim 113 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

122. (Previously presented) The method of claim 114 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

123. (Previously presented) The method of claim 115 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

124. (Previously presented) The method of claim 116 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

125. (Currently amended) The ~~mouse<sup>rodent</sup>~~ of claim 77 84 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

126. (Currently amended) The ~~mouse<sup>rodent</sup>~~ of claim 125 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.

127. (Currently amended) The ~~mouse<sup>rodent</sup>~~ of claim 77 84 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

128. (Currently amended) The ~~mouse<sup>rodent</sup>~~ of claim 78 82 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

129. (Currently amended) The ~~mouse/rodent~~ of claim 128 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.

130. (Currently amended) The ~~mouse/rodent~~ of claim ~~78~~ 82 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

131. (Currently amended) The ~~mouse/rodent~~ of claim ~~79~~ 83 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

132. (Currently amended) The ~~mouse/rodent~~ of claim 131 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.

133. (Currently amended) The ~~mouse/rodent~~ of claim ~~79~~ 83 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

134. (Currently amended) The ~~mouse/rodent~~ of claim ~~80~~ 84 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

135. (Currently amended) The ~~mouse/rodent~~ of claim 134 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.

136. (Currently amended) The ~~mouse/rodent~~ of claim ~~80~~ 84 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

137-140. (Cancelled)